Human Spaceflight Capabilities

Mathematical Modeling of Circadian/Performance Countermeasures

Completed Technology Project (2004 - 2008)

Project Introduction

We developed and refined our current mathematical model of circadian rhythms to incorporate melatonin as a marker rhythm. We used an existing physiologically based mathematical model of the diurnal variations in plasma melatonin levels. The revised model can predict melatonin amplitude, markers of melatonin phase (melatonin synthesis onset (Synon) and synthesis offset (Synoff)), melatonin suppression by light, and salivary melatonin concentrations. Our model has been validated on several independent data sets. A manuscript of this work has been published. We incorporated wavelength sensitivity into our current mathematical model. We have revised the light input to our model from lux to an irradiance measure (microW/cm2) for both polychromatic and monochromatic light exposures. We have developed a two-channel photoreceptor model, in which one channel is driven by rod/cone input and the other channel is driven by a melanopsin input with peak sensitivity in the short wavelength range (~480nm). Our model can predict the response of the circadian pacemaker to 1-pulse light exposures of 460nm and 555nm at different irradiances to generate fluence-response curves of circadian phase-shifts to polychromatic light. This work has been presented at scientific meetings. A manuscript of this work is in preparation. We developed schedule assessment and countermeasure design software. We have developed a schedule/countermeasure design program that allows a user to interactively design a schedule and to automatically design a mathematically optimal countermeasure regime (intensity, duration, and placement). We have demonstrated this tool to NASA personnel. We have substantially redesigned the user interface for CPSS, the software implementation of our mathematical model, based on feedback from NASA users and operational requirements. We have shown that our methods can be used to design a variety of schedules and countermeasures relevant to NASA operations including shifting sleep wake (slam shifting), sleep deprivation, and non-24 hour schedules. This work has been presented at scientific meetings. A manuscript is in progress. We have begun to explore inter-individual differences in performance. (1) We have begun developing methodologies for determining how optimal model structure may differ by individual. The benefit of the framework is that models are easily understandable by non-mathematicians and that the probability distributions can be approximated by existing data. (2) We have conducted data analysis to quantify differences in model parameter values and we have correlated these model parameter differences with individual characteristics such as age, gender, morningness-eveningness, habitual bedrest duration, and habitual sleep/wake times. We have demonstrated the trait-like characteristics in the robustness of parameters associated with the homeostatic process under experimental light interventions. This work has been presented at scientific meetings.

Anticipated Benefits

The development (1) of mathematical models of circadian rhythms, sleep,

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alertness, and performance and (2) of software based on these models that aid in schedule design can improve performance and alertness and thereby effectiveness and public safety for people who work at night, on rotating schedules, on non-24-hr schedules or extended duty schedules (pilots, train and truck drivers, shift workers, health care workers, public safety officers, etc.). Attempting to sleep at adverse circadian phases is difficult and sleep efficiency is poor. Attempting to work at adverse circadian phases and/or after long durations of time awake results in poor worker performance and productivity, increased accidents, and decreased safety for workers and for others affected by the workers. For example, the accidents at the Chernobyl and Three Mile Island nuclear reactors and the Exxon Valdez grounding all were partially caused by workers working at adverse circadian phases (~ 4 am). The mathematical modeling and the available Circadian Performance Simulation Software (CPSS) can be used to simulate and quantitatively evaluate different scenarios of sleep/wake schedules and light exposure to predict the resulting circadian phase and amplitude, subjective alertness, and performance. CPSS has been requested by members of academia, government, and industry (transportation (especially airline personnel), safety, medical, military). Its use could help produce improved schedules for working for people in space and on Earth. The software also now includes optimal countermeasure design, so that countermeasures can be planned for times of predicted poor performance and alertness. The schedule/countermeasure design program allows a user to interactively design a schedule and to automatically design a mathematically optimal countermeasure regime (intensity, duration, and placement). This will be valuable to those who schedule people who work at night, on rotating schedules, on non-24-hr schedules, or extended duty schedules. Individuals can design countermeasures for their assigned work schedules so that their sleep and wake rhythms will be adjusted for optimal performance at desired times. Using these tools, we have completed systematic simulation studies of the effect of circadian shifting on phase re-entrainment and performance recovery. For example, we examined the effect of light levels within cockpits and passenger cabins on circadian phase and performance during trans-meridian travel and polar flight paths for an article that appeared in The Wall Street Journal in 2004. The mathematical modeling has been used for basic scientific research. Inclusion of mathematical models in the planning process to optimize measures to be studied in experimental protocols enables more efficient use of research resources and directs new research. If the modeling of existing data is unsatisfactory, then the model assumptions need to be revised. This revision may include identification of a new physiological process not previously described. As an example, an additional component (non-linear response to ocular light stimuli) was added to the circadian rhythms component of our mathematical model to describe data collected in our clinical research facilities, even before the anatomic and physiologic basis of this component of the mathematical model was found. Later experiments validated this mathematical finding. The mathematical model had demonstrated that previously unknown additional physiological processes were involved. The

Organizational Responsibility

Responsible Mission Directorate:

Space Operations Mission Directorate (SOMD)

Lead Center / Facility:

Johnson Space Center (JSC)

Responsible Program:

Human Spaceflight Capabilities

Project Management

Program Director:

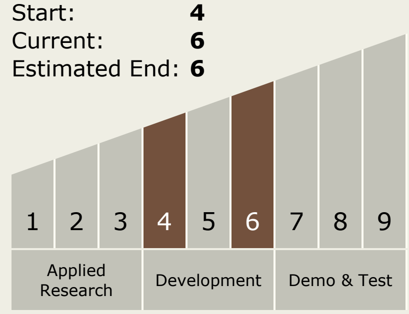
David K Baumann

Principal Investigator:

Elizabeth B Klerman

Technology Maturity (TRL)

Start: **4**
Current: **6**
Estimated End: **6**



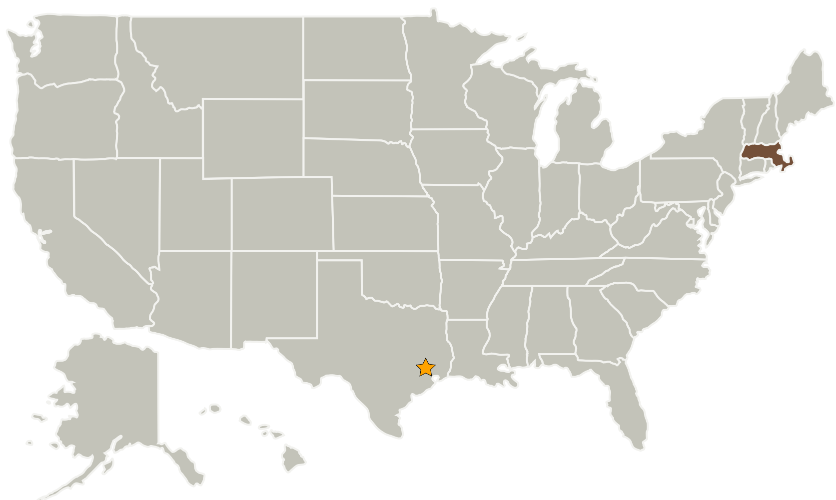
Technology Areas

Primary:

Continued on following page.

modeling work on the differential effects of different wavelength of light on circadian rhythms and alertness can be used for designing artificial (indoor) lighting systems that can maximize circadian or alerting response. The mathematical modeling efforts and CPSS have also been used in educational programs and in the popular press to teach students and teachers about circadian rhythms and sleep and their effects on alertness and performance.

Primary U.S. Work Locations and Key Partners



Organizations Performing Work	Role	Type	Location
★Johnson Space Center(JSC)	Lead Organization	NASA Center	Houston, Texas
Brigham And Women's Hospital, Inc.	Supporting Organization	Industry	Boston, Massachusetts

Primary U.S. Work Locations
Massachusetts

Technology Areas *(cont.)*

- TX06 Human Health, Life Support, and Habitation Systems
  - └ TX06.3 Human Health and Performance
    - └ TX06.3.2 Prevention and Countermeasures

Target Destinations

The Moon, Mars

Project Transitions

June 2004: Project Start

August 2008: Closed out

Closeout Summary: We developed and refined our current mathematical model of circadian rhythms to incorporate melat onin as a marker rhythm. We used an existing physiologically based mathematical model of the diurnal variations in plasma melatonin levels. The revised model can predict melatonin amplitude, markers of melatonin phase (melatonin synthesis ons et (Synon) and synthesis offset (Synoff)), melatonin suppression by light, and salivary melatonin concentrations. Our mode l has been validated on several independent data sets. A manuscript of this work has been published. We incorporated wav elength sensitivity into our current mathematical model. We have revised the light input to our model from lux to an irradia nce measure (microW/cm2) for both polychromatic and monochromatic light exposures. We have developed a two-channel photoreceptor model, in which one channel is driven by rod/cone input and the other channel is driven by a melanopsin inp ut with peak sensitivity in the short wavelength range (~480nm). Our model can predict the response of the circadian pace maker to 1-pulse light exposures of 460nm and 555nm at different irradiances to generate fluence-response curves of circa dian phase-shifts to polychromatic light. This work has been presented at scientific meetings. A manuscript of this work is i n preparation. We developed schedule assessment and countermeasure design software. We have developed a schedule/co untermeasure design program that allows a user to interactively design a schedule and to automatically design a mathemat ically optimal countermeasure regime (intensity, duration, and placement). We have demonstrated this tool to NASA person nel. We have substantially redesigned the user interface for CPSS, the software implementation of our mathematical model, based on feedback from NASA users and operational requirements. We have shown that our methods can be used to design a variety of schedules and countermeasures relevant to NASA operations including shifting sleep wake (slam shifting), sleep deprivation, and non-24 hour schedules. This work has been presented at scientific meetings. A manuscript is in progress. We have begun to explore inter-individual differences in performance. (1) We have begun developing methodologies for det ermining how optimal model structure may differ by individual. The benefit of the framework is that models are easily unde rstandable by non-mathematicians and that the probability distributions can be approximated by existing data. (2) We have conducted data analysis to quantify differences in model parameter values and we have correlated these model parameter differences with individual characteristics such as age, gender, morningness-eveningness, habitual bedrest duration, and ha bitual sleep/wake times. We have demonstrated the trait-like characteristics in the robustness of parameters associated wit h the homeostatic process under experimental light interventions. This work has been presented at scientific meetings.

Stories

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Project Website:

https://taskbook.nasaprs.com